

## Is there a CASTLE-AF on the hill?

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## **Is there a CASTLE-AF on the hill? Additional evidence supporting atrial fibrillation ablation in patients with symptomatic atrial fibrillation and heart failure.**

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Atrial fibrillation is common in patients with heart failure and is associated with a worse outcome. Previous studies of rhythm control using antiarrhythmic drugs have not shown any prognostic benefit in atrial fibrillation.<sup>1,2</sup> Even in patients with heart failure, the large Atrial Fibrillation Congestive heart failure trial failed to show a benefit of amiodarone despite a marked reduction in atrial fibrillation burden.<sup>3</sup> It has been suggested that antiarrhythmic drugs alone may not be powerful enough to maintain sinus rhythm, particularly in heart failure, or that the beneficial effects of sinus rhythm in this group are balanced by the adverse effects of antiarrhythmic drugs.

Ablation offers a powerful treatment to restore sinus rhythm and reduce recurrent atrial fibrillation without requiring long-term therapy, and with synergistic effects on top of antiarrhythmic drugs. Early studies suggested improved exercise tolerance with atrial fibrillation ablation in patients with heart failure.<sup>4</sup> The PABA-CHF pilot trial in 2008 compared pulmonary vein isolation to AV node ablation and biventricular pacing in patients with atrial fibrillation and severe heart failure. Ablation led to greater improvements in exercise tolerance, ejection and symptoms.<sup>5</sup> More recently the AATAC study comparing ablation with amiodarone in persistent atrial fibrillation confirmed these findings and also appeared to show reduced mortality in the ablation group.<sup>6</sup>

The recently published CASTLE AF study is the largest study comparing rhythm control therapy by ablation to rate control therapy in patients with atrial fibrillation and heart failure. Over 350 patients were randomised and followed up for over 3 years. Patients were included if they had evidence of symptomatic atrial fibrillation and an ejection fraction less than 35% and either an implanted defibrillator or CRT-D. The vast majority had either paroxysmal atrial fibrillation or persistent atrial fibrillation of less than one year. They also had to be intolerant of, unresponsive to, or unwilling to take antiarrhythmic drugs. Patients were randomized to ablation or to rate control therapy.

The initial findings of CASTLE – AF are extremely impressive. Ablation led to an improvement in ejection fraction, and a transient but not sustained improvement in 6 minute walk. More importantly ablation was associated with a significant reduction in mortality (13.4% compared 25%) and hospitalisation associated with heart failure, but had no effect on all cause hospitalization or stroke rate. This is extremely encouraging and suggests a benefit of ablation in patients with atrial fibrillation and heart failure.

**Comment [PK1]:** Can you double check this please

The use on intracardiac signals to monitor rhythm also showed the effectiveness of ablation to prevent recurrent atrial fibrillation. The mean atrial fibrillation burden in the ablation group was less than 30% with 81% having less than 5%. In contrast, 56% of the patients randomised to antiarrhythmic drugs were in persistent atrial fibrillation at the end of the trial.

There are however a number of important caveats before rolling out ablation to all patients with AFib and heart failure. All the patients in the CASTLE-AF trial had symptomatic AFib and the majority had previously failed antiarrhythmic drug treatment. Over 3000 patient had to be screened to identify 363 patients to take part in the trial. The quality of the rate control in the pharmacological group has not been published and there were still active attempts to maintain sinus rhythm in this group. AV nodal ablation was rarely used in CASTLE-AF<sup>7</sup> Indeed at 5 years, 20% of the patients randomized to pharmacological rate control were still in sinus rhythm and only 56% had persistent atrial fibrillation. The mortality benefits of ablation only appeared relatively late on in the trial by which stage only 191 of the original trial patients were still being followed up. There were potentially significant differences in patient characteristics between the groups, with a greater incidence of diabetes and ischaemic cardiomyopathy. Some sub-groups also appeared to do less well with ablation. In particular patients with an ejection fraction of less than 25% appeared to have no benefit from ablation.

**Half-way up the hill.** In conclusion, the CASTLE AF study further substantiates earlier reports that atrial fibrillation ablation is beneficial in a highly selected group of patients with atrial fibrillation and severe heart failure in whom antiarrhythmic drugs are not tolerated or ineffective. Further trials need to report before the widespread adoption of an ablation strategy for all patients with atrial fibrillation and heart failure. Data from the CABANA trial, possibly expected later this year, will provide information on the relative safety of ablation compared to antiarrhythmic drugs in a wider group of AF patients. The EAST AFNET 4 trial will provide further evidence of the potential prognostic benefits of early rhythm control soon after the diagnosis of fibrillation. Until this and other information is available, it seems worth to consider atrial fibrillation ablation in patients with symptomatic atrial fibrillation and severe heart failure on top of device therapy.

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